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10/565,161	01/19/2006	Pnina Fishman	FISHMAN19A	7305

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	
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11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,161	FISHMAN ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/25/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,37 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 07/25/08.

The amendment filed 08/25/08 affects the application, 10/565,161 as follows:

1. Claims 1, 10, 12, 13 have been amended. New Claims 37-38 have been have been added. Applicant amendments have overcome the Claims objection of the prior office action mailed 01/25/08. Consequently, the said objection is withdrawn. However, the rejections made under 35 U.S.C. 112, first paragraph and under 35 U.S.C. 103(a) are maintained
2. The responsive to applicants' amendment and arguments is contained herein below.

Claims 1-21, 37-38 are pending in application

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21, 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 12 and 13 recite the phrase "significantly larger". However, the claim is indefinite since it is unclear what value, quantity, amount, factor or difference constitutes a "significantly larger" anti-inflammatory effect.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21, 37-38 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the instant method of treating specific types of inflammatory condition or diseases such as arthritis or rheumatoid arthritis in a subject, does not reasonably provide enablement for treating all types or any type of inflammatory diseases or conditions, as encompassed by the claims, by administering a given composition or compound(s).

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating a subject having an inflammatory condition, comprising administering to the subject a combination of an effective amount of methotrexate (MTX) and an effective amount of an agonist of the A3 adenosine receptor (A3AR agonist).

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on treating all or any of the numerous inflammatory conditions or diseases as recited in claims 1, 12 and 13 herein.

Regarding the *Wands* factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses all or any of the vast number of inflammatory diseases or conditions which include arthritis, pulmonary diseases, psoriasis, colitis, multiple sclerosis, systematic lupus erythematosus, juvenile diabetes, atherosclerosis, hypothyroidism, tonsillitis, pharyngitis, otitis media, pharyngitis, inflammatory bowel disease, bronchitis, inflammatory diseases of the central nervous system such as algal disorders, bacterial disorders, idiopathic Inflammatory disorders, parasitic encephalomyelitis and viral disorders, which are known to involve various, many possible, different, separate and independent, even unknown pathology, etiologies, or symptoms. The treatment some of inflammatory diseases may require more than one distinct, separate, and independent methods, and regimens. For example, Pelvic inflammatory disease is often caused by a combination of different types of bacteria, so a combination (regimen) of medications is used to treat the infection or disease.

The skilled artisan would view the treating of all or any of the vast number of inflammatory diseases, by administering the VERY same compound, as being **highly *unpredictable***.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary:

In the instant case, **no** working examples are presented in the specification as filed showing how to treat inflammatory conditions or diseases other than arthritis or rheumatoid arthritis, i.e., no testing results provided for inflammatory conditions or diseases other than arthritis or rheumatoid arthritis.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad treatment of all or any inflammatory disease encompassed by the instant claims. As a result, necessitating one of skill to perform an exhaustive search and undue experimentation for the embodiments of treating all or any inflammatory diseases recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success. It should be noted that the method of alleviating the inflammatory response in a subject having an inflammatory condition is also encompassed by this rejection since the alleviation of inflammatory response also pertains to all inflammatory conditions.

Claims 9, 10, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the instant method of treating specific types of autoimmune disease such as arthritis and rheumatoid arthritis in a subject, does not reasonably provide enablement for treating all types or any type of autoimmune diseases, as encompassed by the claims, by administering a given composition or compound(s).

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating an autoimmune condition or disease in a subject in need thereof, comprising administering to the subject an effective amount of the said composition or compound(s).

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on treating all or any of the numerous autoimmune diseases recited in claims 9, 10, 20 and 21 herein.

Regarding the *Wands* factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses all or any of the autoimmune disease such as systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, scleroderma, pernicious anemia, myasthenia gravis, and Hashimoto's disease, which are known to involve various, many possible, different, separate and independent, even unknown pathology, etiologies, or symptoms. The method for the treatment of an autoimmune disease is not one but at least two distinct, separate, and independent methods. For example, as defined by Ninham et at. (WO 85/05031, PTO-892), the immune response in a human or animal subject can be suppression or enhancement (see page 1-2). Autoimmune diseases can be treated by artificial suppression (immunosuppression) or enhancement (immunopotentation), wherein these two treatments are involved in distinct and separate agents, processes and mechanisms, and most importantly which are in both opposite directions.

"To date, immunosuppressive drugs that have been developed to manipulate the immune response, are usually compounds of complex structure that have been discovered by accident. Further, their mode of action is often unknown or very unpredictable and administration of drugs can be accompanied by undersirable side-effects" (emphasis added). See page 2, in particular line 19-25.

The skilled artisan would view that the treating any autoimmune diseases, encompassing both suppression (immunosuppression) and enhancement (immunopotentation), by administering the

VERY same compound, as being **highly *unpredictable***. Therefore, the skilled artisan would view that the treatment of all autoimmune diseases herein, by administering the same compound herein, is highly *unpredictable*.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary: In the instant case, **no** working examples are presented in the specification as filed showing how to treat autoimmune disease other than arthritis or rheumatoid arthritis, i.e., no testing results provided.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad treatment of all or any autoimmune disease encompassed by the instant claims. As a result, necessitating one of skill to perform an exhaustive search and undue experimentation for the embodiments of treating all or any autoimmune diseases recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jeurissen et al. (Arthritis and rheumatism, 1991 Aug) Vol. 34, No. 8, pages 961-972) in view of et al. Fishman (US 2004/0167094 A1).

In claim 1, applicant claims a method of alleviating the inflammatory response in a subject having an inflammatory condition, comprising administering to the subject a combination of an anti-inflammatory effective amount of methotrexate (MTX) and an anti-inflammatory effective amount of an agonist of the A3 adenosine receptor (A3AR agonist), wherein the combination provides a combined anti-inflammatory effect significantly larger than that provided by either MTX or A3AR agonist used alone. Claims 2-11, 37-38 are drawn said method, wherein the A3AR agonist is administered to specific time per day, specific daily dosages, administered orally, the specific agonist are used, specific treatment is indicated and specific inflammatory condition (rheumatoid arthritis) is treated.

Jeurissen et al. disclose a method of treating a subject having an inflammatory condition (rheumatoid arthritis), comprising administering to the subject a combination of an effective amount of methotrexate (MTX) (see abstract). It should be noted that the treatment of the inflammatory condition encompasses or includes the alleviation of inflammatory response. That is, the alleviation of inflammatory response is a mechanism or effect by which said disease or condition is treated.

The difference between applicant's claimed method and the method taught by Jeurissen et al. is that the applicant also uses an agonist of the A3 adenosine receptor (A3AR agonist) in their composition in addition to the methotrexate (MTX).

Fishman discloses a method of treating inflammatory arthritis (rheumatoid arthritis), by administering to a subject an agonist of the A3 adenosine receptor (A3AR agonist) N6-(3-iodobenzyl)-adenosine 5'-N-methyl-uronamide (IB-MECA) and 2-chloro-N6-(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide (CL-IB-MECA) (see abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Jeurissen et al and Fishman, to treat rheumatoid arthritis (which includes alleviating inflammatory response) in a subject by administering to said subject a composition comprising a combination of methotrexate and an A3AR agonist such as IB-MECA or CL-IB-MECA , since the combination of compounds that are used to treat the same diseases or conditions are well known in the art. More specifically, it is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

One having ordinary skill in the art would have been motivated in view of Jeurissen et al and Fishman, to treat rheumatoid arthritis (which includes alleviating inflammatory response) in a subject by administering to said subject a composition comprising a combination of methotrexate and an A3AR agonist such as IB-MECA or CL-IB-MECA, because a skilled artisan would reasonably be expected to prepare composition comprising a combination of the compounds taught by Jeurissen et al and Fishman., to treat rheumatoid arthritis (which includes

alleviating inflammatory response) based on factors such as type and/or severity of the rheumatoid arthritis. It should be noted that the use of different schedules administrations or dosages are common in the art and is well within the purview of a skilled artisan and depends on factors such as the severity or type of the rheumatoid arthrithis and the weight, age and type of the subject treated. Also, it should be noted that one of ordinary skill in the art would (and it is common in the art to) expect that the combination of said compounds would at least produce an additive effect of the said treatment, especially since this is usually one of the main reasons for making the said combination.

Claim 13 is drawn to a method of treating a subject having an inflammatory condition treatable by an agonist of the A3 adenosine receptor (A3AR agonist), comprising administering to the subject an anti-inflammatory amount of an A3AR agonist, the improvement comprising administering to the subject an anti-inflammatory effective amount of methotrexate (MTX), wherein the combination of treatment with MTX and A3AR agonist provides a combined anti-inflammatory effect significantly larger than that provided by either MTX or A3AR agonist used alone.

Jeurissen et al. disclose a method of treating a subject having an inflammatory condition (rheumatoid arthritis), comprising administering to the subject a combination of an effective amount of methotrexate (MTX) (see abstract).

The difference between applicant's claimed method and the method taught by Jeurissen et al. is that the applicant also uses an agonist of the A3 adenosine receptor (A3AR agonist) in their composition in addition to the methotrexate (MTX).

Fishman discloses a method of treating inflammatory arthritis (rheumatoid arthritis), by administering to a subject an agonist of the A3 adenosine receptor (A3AR agonist) N6-(3-iodobenzyl)-adenosine 5'-N-methyl-uronamide (IB-MECA) and 2-chloro-N6-(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide (CL-IB-MECA) (see abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Jeurissen et al and Fishman, to treat rheumatoid arthritis in a subject by administering to said subject a composition comprising a combination of methotrexate and an A3AR agonist such as IB-MECA or CL-IB-MECA , since the combination of compounds that are used to treat the same diseases are well known in the art. More specifically, it is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

One having ordinary skill in the art would have been motivated in view of Jeurissen et al and Fishman, to treat rheumatoid arthritis in a subject by administering to said subject a composition comprising a combination of methotrexate and an A3AR agonist such as IB-MECA or CL-IB-MECA, because a skilled artisan would reasonably be expected to prepare composition comprising a combination of the compounds taught by Jeurissen et al and Fishman., to treat rheumatoid arthritis based on factors such as type and/or severity of the rheumatoid arthritis. It should be noted that the use of different schedules administrations or dosages are common in the art and is well within the purview of a skilled artisan and depends on factors such as the severity or type of the rheumatoid arthrithis and the weight, age and type of the subject treated. Also, it should be noted that one of ordinary skill in the art would (and it is common in

the art to) expect that the combination of said compounds would at least produce an additive effect of the said treatment, especially since this is usually one of the main reasons for making the said combination.

Claims 12, 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fishman (US 2004/0167094 A1) in view of Jeurissen et al. (Arthritis and rheumatism, 1991 Aug) Vol. 34, No. 8, pages 961-972).

Claim 12 is drawn to a method of treating a subject having an inflammatory condition treatable by methotrexate (MTX), comprising administering to the subject an anti-inflammatory amount of MTX, the improvement comprising administering to the subject an anti-inflammatory effective amount of an agonist of the A_3 adenosine receptor (A_3AR agonist), wherein the combination of treatment with MTX and A_3AR agonist provides a combined anti-inflammatory effect significantly larger than that provided by either MTX or A_3AR agonist used alone. Claims 14-21 are drawn said method, wherein the A3AR agonist is administered to specific time per day, specific daily dosages, administered orally, the specific agonist are used and specific inflammatory condition (rheumatoid arthritis) is treated.

Fishman discloses a method of treating inflammatory arthritis (rheumatoid arthritis), by administering to a subject an agonist of the A3 adenosine receptor (A3AR agonist) N6-(3-iodobenzyl)-adenosine 5'-N-methyl-uronamide (IB-MECA) and 2-chloro-N6-(3-iodobenzyl)-adenosine-5'-N-methyl-uronamide (CL-IB-MECA) (see abstract).

The difference between applicant's claimed method and the method taught by Fishman is that Fishman do not disclose that the said subject that is treated with the A3AR agonist is also being treated with methotrexate (MTX).

Jeurissen et al. disclose a method of treating a subject having an inflammatory condition (rheumatoid arthritis), comprising administering to the subject a combination of an effective amount of methotrexate (MTX) (see abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Fishman and Jeurissen et al., to treat rheumatoid arthritis in a subject by administering to the said subject an A3AR agonist such as IB-MECA or CL-IB-MECA, regardless of whether the subject is being treated with MTX and especially since Jeurissen et al. disclose that methotrexate (MTX) can be used to treat inflammatory condition (rheumatoid arthritis), and since the administration of different drugs or compounds to treat the same condition in the same patient is common in the art and is well within the purview.

One having ordinary skill in the art would have been motivated in view of Fishman and Jeurissen et al., to treat rheumatoid arthritis in a subject by administering to the said subject an A3AR agonist such as IB-MECA or CL-IB-MECA, regardless of whether the subject is being treated with MTX, because a skilled artisan would reasonably be expected additional compounds such Fishman's A3AR agonist, to treat rheumatoid arthritis (the same condition or disease) based on factors such as type and/or severity of the rheumatoid arthritis. It should be noted that the use of different schedules administrations or dosages are common in the art and is well within the purview of a skilled artisan and depends on factors such as the severity or type of the rheumatoid arthrithis and the weight, age and type of the subject treated. It should be noted that

the administration of different drugs or compounds to treat the same condition in the same patient is common in the art and is well within the purview of a skilled artisan and depends on factors such as the severity or type of the rheumatoid arthritis and the weight, age and type of the subject treated. Also, it should be noted that one of ordinary skill in the art would (and it is common in the art to) expect that the combination of said compounds would at least produce an additive effect of the said treatment, especially since this is usually one of the main reasons for making the said combination.

Response to Arguments

Applicant's arguments with respect to claims 1-21, 37-38 have been considered but are not found convincing.

The applicant argues the present claims have now been amended to clarify that they are for treating the inflammatory response in a subject having an inflammatory condition. This language is supported, for example, at page 9, lines 8-10, of the present specification, where it states that the term "anti-inflammatory" denotes the disease modifying effect achieved by the combined treatment "in alleviating the inflammatory response in inflammatory conditions." This inflammatory response is a symptom of the inflammatory condition that is being treated. Thus, applicant makes no claim to being able to cure any disease. Applicant's only claim is that the inflammatory response in the inflammatory condition can be alleviated by means of the present invention. Note that at page 9, lines 17-22, the term "inflammatory condition" is defined as one that is characterized by a persistent inflammatory response with pathological sequelae.

However, it should be noted that the treatment of the inflammatory condition encompasses or includes the alleviation or treatment of inflammatory response. That is, the

alleviation of inflammatory response is a mechanism or effect by which said disease or condition is treated. Furthermore, it should be noted that the subject treated must possess an inflammatory condition in order for said alleviation of the inflammatory response to occur by said treatment in said subject. In other word, the inflammatory response does not occur without the presence of the said inflammatory condition. In addition, it is important to note that the specification does not define the term "inflammatory condition" with reasonable clarity, deliberateness, and precision necessary for departure from ordinary meaning. For example, in one of its definition the specification states that the term *"inflammatory condition"* may include a variety of conditions associated with inflammatory responses and immune induced pathologies mediated (e.g. autoimmune disorders) by the immune system (see page 9, last paragraph). It should be noted that in Abbott Laboratories v. Syntron Bioresearch Inc., 67 USPQ2d 1337 (CA FC 2003), the

> **"Term "analyte," as used in claims of patent for chemical analysis apparatus and method, should be given plain meaning adopted by federal district court, namely, "the substance that the test is designed to detect if present in the liquid being tested," even though patentee defined "analyte" in specification, since specification provides two alternative definitions for term, and thus does not define term with reasonable clarity, deliberateness, and precision necessary for departure from ordinary meaning."** See Abbott Laboratories v. Syntron Bioresearch Inc., 67 USPQ2d 1337 (CA FC 2003).

The applicant argues that at page 9, lines 17-22, the term "inflammatory condition" is defined as one that is characterized by a persistent inflammatory response with pathological sequelae. Thus, while the inflammatory condition may have any pathology or etiology, the inflammatory response is expected to be the same and it is this inflammatory response that is being treated. However, the specification also states that the term *"inflammatory condition"* may

include a variety of conditions associated with inflammatory responses and immune induced pathologies mediated (e.g. autoimmune disorders) by the immune system (see page 9, last paragraph). Also, the specification also states that without being limited thereto, in the context of the present invention, inflammatory conditions include psoriasis, psoriatic arthritis, Crohn's disease, rheumatoid arthritis as well as other rheumatic diseases, including polymyositis and systemic lupus erythematosus (see page 9, last paragraph to page 10). Furthermore, inflammatory response involves is a series of local cellular and vascular responses that involves different mediators and thus is not expected to be the same as applicant argues.

The applicant argues that all of the claims have now been amended to specify that the combination of MTX and A3AR agonist provides a combined anti-inflammatory effect significantly larger than that provided by either MTX or A3AR agonist used alone. In other words, synergistic results are obtained that would not have been expected by one of ordinary skill in the art familiar with the anti-inflammatory mechanism of action of MTX. However, one of ordinary skill in the art would (and it is common in the art to) expect that the combination of said compounds would at least produce an additive effect of the said treatment, especially since this is usually one of the main reasons for making the said combination. In addition it should be noted that applicant has not claimed or demonstrated synergistic effect in their specification.

The applicant argues that based on the earlier publications of Dr. Cronstein, it would not have been expected that an additive anti-inflammatory effect could be obtained with administering to the subject an agonist to adenosine. See particularly, paragraphs 11 and 12 of the Cronstein declaration. However, the above rejections are not made over the said publications (see above rejection).

The Declaration under 37 CFR 1.132 filed 07/25/08 is not sufficient to overcome the rejection of claims 1-21, 37-38 based upon Jeurissen et al. and Fishman as applied under U.S.C. 103 (a). The Declaration argues that there was no publication that could have led someone to suspect that MTX and an A3AR agonists such as IB-MECA would lead to a greater anti-inflammatory effect than each of these agents alone. However, one of ordinary skill in the art would (and it is common in the art to) expect that the combination of said compounds would at least produce an additive effect of the said treatment, especially since this is usually one of the obvious or main reasons for making the said combination. In addition, it should be noted that applicant has not claimed or demonstrated synergistic effect in their specification. Furthermore, the above rejections are not made over Jeurissen et al. and Fishman and not the said publications (see above rejection). The Declaration argues that it would not have been expected that an additive anti-inflammatory effect could be obtained with administering to the subject an agonist to adenosine. However, the above rejections are not made over Jeurissen et al. and Fishman and not the said publications (see above rejection).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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November 9, 2008.

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